and who recover quickly with few side effects should be more likely to be discharged if their injuries are of the same severity as those given morphine. The authors may be right in suggesting that this trend will disappear in larger studies.

The message from the paper is clear. Clinical evidence from other settings has shown that ketorolac and morphine are equivalent in relieving pain, but there is a distinct benefit favouring ketorolac in terms of side effects. This was not enough to change clinical practice, probably because of the cost of the drug. This latest evidence that the costs and benefits are also likely to favour ketorolac-with the attendant advantages in efficiency, quality of care, and patient satisfactionshould encourage emergency and primary care physicians to use titrated intravenous ketorolac for severe pain in isolated limb injuries. Given its previously reported efficacy as an analgesic for other conditions in the emergency department, the accumulating weight of evidence suggests that intravenous ketorolac will become the analgesic of choice for many emergencies.

George A Jelinek *Professor of emergency medicine* Sir Charles Gairdner Hospital, Nedlands, Western Australia 6009 (g.jelinek@one.net.au)

- 1 Tramer MR, Williams JE, Carroll D, Wiffen PJ, Moore RA, McQuay HJ. Comparing analgesic efficacy of non-steroidal anti-inflammatory drugs given by different routes in acute and chronic pain: a qualitative systematic review. Cochrane Database of Abstracts of Reviews of Effectiveness. The Cochrane Library, 1999. CRD database number: DARE-980293
- 2 Gillis JC, Brogden RN. Ketorolac. A reappraisal of its pharmacodynamic and pharmacokinetic properties and therapeutic use in pain management. *Drugs* 1997;53:139-88.
- 3 Strom BL, Berlin JA, Kinman JL, Spitz PW, Hennessy S, Feldman H, et al. Parenteral ketorolac and risk of gastrointestinal and operative site bleeding. A postmarketing surveillance study. JAMA 1996;275:376-82.
- 4 Rainer TH, Jacobs P, Ng YC, Cheung NK, Tam M, Lam PKW, et al. Cost effectiveness analysis of intravenous ketorolac and morphine for treating pain after limb injury: double blind randomised controlled trial. BMJ 2000;321:1247-51.
- 5 Jelinek GA. Casemix classification of patients attending hospital emergency departments in Perth, Western Australia. Development and evaluation of an urgency-based casemix information system for emergency departments [thesis]. University of Western Australia, 1995.
- 6 Erwich-Nijhout MA, Bond MJ, Phillips DG, Baggoley C. The identification of costs associated with emergency department attendances. *Emerg Med* 1997;9:181-8.
- 7 Krochmal P, Riley TA. Increased health care costs associated with ED overcrowding. Am J Emerg Med 1994;12:265-6.
- 8 Derlet RW, Richards JR. Overcrowding in the nation's emergency departments: complex causes and disturbing effects. Am Emerg Med 2000;35:63-8.
- 9 Shih FY, Ma MH, Chen SC, Wang HP, Fang CC, Shyu RS, et al. ED overcrowding in Taiwan: facts and strategies. Am J Emerg Med 1999;17:198-909
- 10 Jelinek GA, Baggoley CJ. Financial incentives to change emergency service performance. Med J Aust 1999;171:231-2.

The importance of injecting vaccines into muscle

Different patients need different needle sizes

ost vaccines should be given via the intramuscular route into the deltoid or the anterolateral aspect of the thigh. This optimises the immunogenicity of the vaccine and minimises adverse reactions at the injection site. Recent studies have highlighted the importance of administering vaccines correctly.¹⁻³ Clinical practice needs to reflect considerations about the right length and gauge of needles used to ensure that those vaccinated get the immunological benefit of the vaccines without local side effects.

Injecting a vaccine into the layer of subcutaneous fat, where poor vascularity may result in slow mobilisation and processing of antigen, is a cause of vaccine failure¹—for example in hepatitis B,² rabies, and influenza vaccines.³ Compared with intramuscular administration, subcutaneous injection of hepatitis B vaccine leads to significantly lower seroconversion rates and more rapid decay of antibody response.¹

Traditionally the buttocks were thought to be an appropriate site for vaccination, but the layers of fat do not contain the appropriate cells that are necessary to initiate the immune response (phagocytic or antigenpresenting cells). The antigen may also take longer to reach the circulation after being deposited in fat, leading to a delay in processing by macrophages and eventually presentation to the T and B cells that are involved in the immune response. In addition, antigens may be denatured by enzymes if they remain in fat for hours or days. The importance of these factors is supported by the findings that thicker skinfolds are associated with a lowered antibody response to vaccines. 12

Serious reactions to intramuscular injections are rare; in one series of 26 294 adults, of whom 46% had received at least one intramuscular injection, only 48

(0.4%) had a local adverse effect.⁴ However, subcutaneous injections can cause abscesses and granulomas.^{1 5 6} Muscle is probably spared the harmful effects of substances injected into it because of its abundant blood supply.⁵ Adipose tissue, having much poorer drainage channels, retains injected material for much longer and is therefore also more susceptible to its adverse effects.⁵ In the case of vaccines in which the antigen is adsorbed to an aluminium salt adjuvant—such as those for hepatitis A, hepatitis B, and diphtheria, tetanus, and pertussis vaccines—the intramuscular route is strongly preferred because superficial administration leads to an increased incidence of local reactions such as irritation, inflammation, granuloma formation, and necrosis.^{2 7 8}

The injection technique and needle size both determine how deep a substance is injected. Injection technique involves stretching the skin flat before inserting the needle or pinching a fold of skin before injection, which may necessitate the use of longer needles. To make sure the needle reaches the muscle and that vaccine does not seep into subcutaneous tissue the decision on the size of the needle and injection site should be made individually for each person. It should also be based on the person's age, the volume of material to be administered, and the size of the muscle.⁹

In a recent study, the thickness of the fat pad above the deltoid muscle of the upper arm was measured in 220 adults (healthcare workers presenting for hepatitis B immunisation) using high frequency ultrasonography. A wide variation exists in thickness of the deltoid fat pad, with women having significantly more subcutaneous fat than men. A standard 5/8 inch (16mm) needle would not have achieved sufficient penetration for true deltoid intramuscular injection in

BMJ 2000;321:1237-8

17% of men and nearly 50% of women in the study population. For men weighing 59-118 kg and women of 60-90 kg it may be safer to use a 1 inch (25mm) needle. A woman over 90 kg may need a 1.5 inch (38mm) needle.

Healthcare professionals may hesitate to use longer needles on the grounds that they are likely to cause the patient more discomfort. However, skeletal muscle has a poor supply of pain fibres compared with skin and subcutaneous tissue.¹⁰

Consideration should be given to needle gauge.

A wider bore needle ensures that the vaccine is dissipated over a wider area, thus reducing the risk of localised redness and swelling.

The consideration is a swelling of the risk of localised redness and swelling.

A standard size of needle will not guarantee successful intramuscular injection in all people. When intramuscular vaccine administration is needed to ensure optimal immunogenicity and minimise local reactions, a selection of non-fixed needles (pre-filled syringes that may be provided with a needle fixed on the barrel) should be available to allow healthcare professionals to select a length and gauge of needle appropriate to each patient.

Jane N Zuckerman senior lecturer

Academic Centre for Travel Medicine and Vaccines, Royal Free and University College Medical School, London NW3 2PF (j.zuckerman@rfc.ucl.ac.uk)

JZ has been given financial support from several vaccine manufacturers for attending conferences, organising educational programmes, and for undertaking research.

- Poland GA, Borrud A, Jacobson RM, McDermott K, Wollan PC, Brakke D, et al. Determination of deltoid fat pad thickness: implications for needle length in adult immunization. *JAMA* 1997;277:1709-11.
 Shaw FE Jr, Guess HA, Roets JM, Mohr FE, Coleman PJ, Mandel EJ, et al.
- 2 Shaw FE Jr, Guess HA, Roets JM, Mohr FE, Coleman PJ, Mandel EJ, et al. Effect of anatomic site, age and smoking on the immune response to hepatitis B vaccination. *Vaccine* 1989;7:425-30.
- 3 Groswasser J, Kahn A, Bouche B, Hanquinet S, Perlmuter N, Hessel L. Needle length and injection technique for efficient intramuscular vaccine delivery in infants and children evaluated through an ultrasonographic determination of subcutaneous and muscle layer thickness. *Pediatrics* 1997;100:400-3.
- 4 Greenblatt DJ, Allen M. Intramuscular injection-site complications. JAMA 1978:240:524-4.
- $5\,$ Michaels L, Poole RW. Injection granuloma of the buttock. Can Med Ass J $1970;\!102:\!626\!-\!8.$
- 6 Haramati N, Lorans R, Lutwin M, Kaleya RN. Injection granulomas: intramuscle or intrafat? Arch Fam Med 1994;3:146-8.
- 7 Ipp MM, Gold R, Goldbach M, Maresky DC, Saunders N, Greenberg S, Davy T. Adverse reactions to diphtheria, tetanus, pertussis-polio vaccination at 18 months of age: effect of injection site and needle length. *Pediatris* 1989;83:679-82.
- 8 American Academy of Pediatrics. Report of the committee on infectious diseases. 24th ed. Washington: AAP, 1997.
- 9 Advisory Committee on Immunization Practices (ACIP). General recommendations on immunization. MMWR 1994;43:RR-1:6.
- 10 Greenblatt DJ, Koch-Weser J. Intramuscular injection of drugs. N Engl J $\it Med$ 1976;295:542-6.
- 11 Salisbury DM, Begg NT, eds. Immunisation against infectious diseases. London: HMSO, 1996:16.
- 12 Mayon-White R, Moreton J. Immunizing children. 2nd ed. London Radcliffe, 1998: 28, 43.

Barrett's oesophagus: the continuing conundrum

Surveillance should be confined to the surgically fit

n 1950 Barrett wrote a treatise to clarify confusion over oesophagitis which "connote[s] one thing to some people and something quite different to others." He described gastric mucosa extending into the tubular oesophagus as the result of a congenitally shortened oesophagus. The presence of columnar lined epithelium in the oesophagus is now referred to as Barrett's oesophagus. It is associated with chronic gastro-oesophageal reflux disease and an increased risk of oesophageal adenocarcinoma. Quantifying this risk, and the best methods for early diagnosis, are still the subjects of considerable debate.

Endoscopically the distal end of the pearly white oesophagus is readily distinguished from the salmon red of the proximal stomach: the so called "Z line" or squamocolumnar junction. However, the location of the Z line may be difficult to identify in cases of intense inflammation, hiatal hernia, and stricture patients with oesophagitis. Extension of the Z line proximallyrepresenting columnar replacement of the squamous epithelium of the distal oesophagus (Barrett's oesophagus)—is seen in 5-15% of patients with peptic oesophagitis.² Historically one point of confusion has been whether a minimal length of columnar metaplasia is needed to qualify for the diagnosis of Barrett's oesophagus: is it >2 cm, >3 cm, or >5 cm? In part, these arbitrary criteria were established to avoid "false positive" biopsies of intestinal metaplasia which often occur in the gastric cardia. The requirement of a minimum length to establish Barrett's oesophagus has been abandoned. Histologically, the columnar based epithelium can be one of three types: gastric fundic gland, junctional type epithelium with cardiac mucous glands, or a distinct type of columnar metaplasia called specialised columnar (intestinal) epithelium.³ Only patients who have the specialised columnar epithelium are at an increased risk of cancer and should be considered for endoscopic surveillance.

About 10% of patients who have Barrett's oesophagus at the time of the initial endoscopic examination have coexistent oesophageal adenocarcinoma. ^{4 5} The incidence of oesophageal adenocarcinoma has rapidly increased over the past two decades in Western Europe and the United States. ⁶ Unfortunately, the 5 year survival rate is 11%. The risk factors for this cancer are longstanding gastro-oesophageal reflux disease, the presence of Barrett's specialised columnar epithelium, male sex, and white race. ^{6 7} In a case-control study Lagergren et al showed that a greater risk of oesophageal adenocarcinoma was associated with more frequent, more severe, and longer lasting symptoms of acid reflux. ⁷

It is difficult to know how to avoid the dismal prognosis of advanced cancer in patients with Barrett's oesophagus. Earlier reports from prospective studies showed that about one adenocarcinoma developed for every 100 patient years, representing a 30-fold to 125-fold increase in the risk of cancer compared with the general population.² It is also believed that in patients with Barrett's oesophagus the development of adenocarcinoma is preceded by a continuum of dysplasia, from low to high grade, that can be readily identified by

papers p 1252

BMJ 2000;321:1238-9